

ACID CATALYZED CONDENSATIONS OF CYCLIC
KETONES: I. ATTEMPTED SYNTHESIS OF
PHENANTHRENE

by

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INTRODUCTION

Polycyclic hydrocarbons and their derivatives constitute a portion of organic chemistry that has received a good deal of attention, both synthetically and theoretically. Although little practical value may be derived from most of the hydrocarbons themselves in an economic sense, many of their derivatives find a great deal of use in various fields. This is especially true of the lower members of the series, particularly naphthalene, anthracene, and phenanthrene.

Theoretically they have received much attention with relation to structural features, particularly with respect to comparison of the aromatic members with benzene. They generally show a great deal of the resonance energy and the aromatic character so pronounced in benzene. However, they have somewhat lower resonance energy values than benzene.

Economically, derivatives of these compounds find considerable use in various industries such as in the dye and pharmaceutical fields. They form a class of compounds which are, in general, physiologically active and whose activity ranges from carcinogenic character, through hormones and dietary factors, to antibiotics such as aureomycin and terramycin.

Phenanthrene is the lowest member of the angularly condensed hydrocarbons and, although the hydrocarbon itself

has little practical value, its derivatives are quite important in many phases of pharmaceutical chemistry.

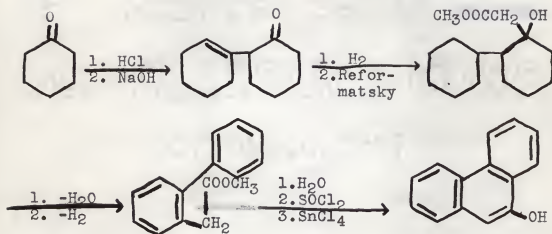
A great many naturally occurring compounds are phenanthrene derivatives. Among these are morphine, codeine, and related alkaloids, the D vitamins, the resin acids, various cardiac active glycosides, and many hormones such as the sex hormones and cortisone. It would be of value, therefore, to develop a general synthesis of substituted phenanthrenes for both synthesis and structure elucidation of these natural products.

This work was carried out both as an attempted method for the preparation of 9-phenanthrol and as part of a long range project involving the application of both the acid catalyzed condensation of cyclic ketones and the Reformatsky reaction to the synthesis of various polycyclic hydrocarbons.

The successful preparation of 9-phenanthrol by the proposed synthesis would open a route to substituted phenanthrenes, especially the 1,5- and 2,6- disubstituted compounds. In addition, it was found during the course of the work that intermediates might be obtained which would lead to the 1,5,9- and 2,6,10- trisubstituted compounds. These substituents are valuable as points of modification of structure as substituents may not be placed in some of these positions by reactions involving phenanthrene itself. Since most substitution reactions of phenanthrene yield rather complex mixtures, with substituents becoming attached

to various points of the nucleus, it is also preferable from the point of yield to synthesize the nucleus with the desired substituents already present.

The original synthesis may be represented as follows:



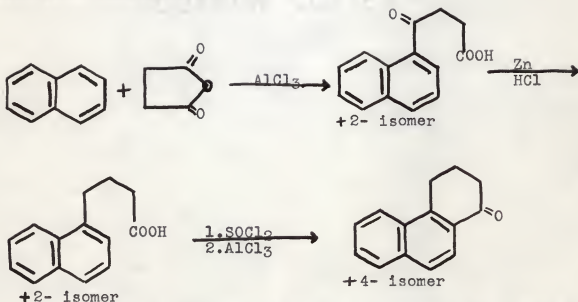
It was found however, that major difficulties were inherent in this scheme, and thus could not be followed completely.

HISTORY

Phenanthrene is a colorless compound, which exhibits a weak blue fluorescence in solution, and melts at 100°C. It may be obtained from the distillation of coal tar. It occurs in the same fraction as anthracene, from which it may be separated by solution in carbon disulfide or pyridine.

There are, at present, several methods for the synthesis of phenanthrene and its derivatives. The easiest of these

is that of Haworth (10), which consists of succinylation of naphthalene followed by a Clemmensen reduction of the keto group and a ring closure of either the acid with sulfuric acid, or the acid chloride with stannic chloride, aluminum chloride, or other Friedel-Crafts catalyst. Succinylation substitutes at both the 1- and 2- positions, but the two acids may be separated rather easily, and in many cases the same final phenanthrene is obtained from both and makes separation unnecessary.

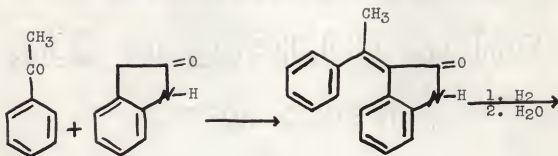


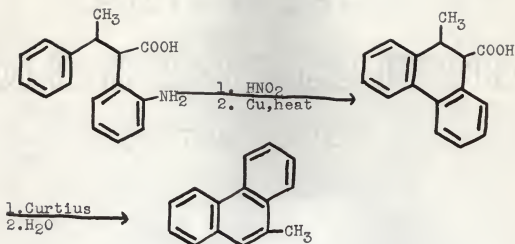
Substituted phenanthrenes may be obtained in many cases by varying the reactants. These fall into three general categories: (a) succinylation of certain substituted naphthalenes, such as the 1- or 2- alkyl compounds, (b) the use of alkyl substituted succinic anhydrides which leads to two products which may in general be separated, and (c) Grignard reactions of either or both of the keto compounds formed as intermediates.

Procedure (a) leads to 9- alkyl substituents if the 1- substituted naphthalene is used, and 1- alkyl phenanthrenes if the 2- substituted naphthalene is used. Procedure (b) leads to 2- and 3- substituted phenanthrenes from the two possible products. It has been found that only two products are formed since the carbonyl group farthest removed from the alkyl group is the one which becomes attached to the ring. Procedure (c) leads to either 1- or 4- substituted phenanthrenes, depending on which isomer is used (8).

The Pschorr (17) synthesis involves a Perkin type condensation of an o-nitrobenzaldehyde with an arylacetic acid as the original step. This is followed by reduction to the amine, diazotization, and thermal ring closure with copper. This method has been modified a good deal by many investigators.

One of the most important of these is the oxindole modification of Windaus and Eickel (22), which leads to 9- substituted phenanthrenes by the following scheme:





Bardhan and Sengupta (3) used an acetoacetic ester alkylation of 2-carbethoxycyclohexanone with 2-phenylethylbromide, followed by a dehydrative ring closure, and Bogert, et al (5) and Cook and Hewett (7) used a Grignard reaction with 2-phenylethylmagnesium bromide and cyclohexanone followed by the same type of dehydrative ring closure. Both of these syntheses are subject to a good deal of modification to obtain various derivatives of phenanthrene.

In 1949, Bagchi, et al (2), synthesized octahydro-9-phenanthrol utilizing the Reformatsky reaction on 2-cyclohexenylcyclohexanone, followed by a dehydrative ring closure. This proved to be the most direct route to this compound and its derivatives known at that time. It therefore seemed reasonable that, with certain modifications, Bagchi's procedure might be adapted to the synthesis of phenanthrene and substituted phenanthrenes. The 2-cyclohexenylcyclohexanone may be readily prepared by the acid catalyzed condensation of cyclohexanone and this procedure may be

readily adapted to the condensation of various substituted cyclohexanones, which are in turn available from the corresponding phenols.

The acid catalyzed ketone condensation has been known for some time, especially in connection with the synthesis of dodecahydrotriphenylene from cyclohexanone and of mesitylene from acetone, through the condensation of three molecules of the ketone. By varying the reaction conditions, however, one may obtain a good yield of the product formed by the condensation of only two molecules of ketone.

Various investigators have proposed methods of synthesis of 2-cyclohexenylcyclohexanone, or its isomer 2-cyclohexylidenecyclohexanone. Of these, that of Rapson (18) is the easiest and affords the cleanest reaction product in the highest yields.

The Reformatsky reaction has been varied likewise a good deal and many procedures are available. One of the best of these is that of Bachmann and Dreiding (1), which involves the addition of zinc and bromoester in small portions to the carbonyl compound while refluxing.

The ring closures of various types that have been used with this type of synthesis vary only in the dehydrating reagent used, with phosphorous pentoxide and sulfuric acid being the most commonly used agents.

EXPERIMENTAL

Preparation of 2-Cyclohexylidenecyclohexanone (I)
by the method of Gault, et al (9)

A mixture of 100 g. of 50 per cent sulfuric acid and 100 g. of cyclohexanone was allowed to stand for twenty-four hours. The mixture was then steam distilled and the distillate salted out with sodium carbonate. The resulting mixture was extracted three times with benzene, the benzene was removed by distillation and the product was distilled under reduced pressure. The fraction boiling at 153-160°C. at 25-29 mm. pressure was collected. This material was a colorless liquid which turned a pale yellow on standing. The yield was 35.2 g. (38.8 per cent).

Preparation of 2-Cyclohexylidenecyclohexanone (I)
by the method of Mannich (14)

To a solution of 54 ml. of concentrated sulfuric acid in 316 ml. of methanol was added 106 ml. of cyclohexanone. The resulting solution was refluxed for ten hours and the product worked up in the same manner as above. A 9 per cent yield of product was obtained.

Preparation of 2-Cyclohexenylcyclohexanone (II)

Anhydrous hydrogen chloride was passed into 28.5 g. of cyclohexanone until saturated. The mixture was allowed to

stand for one hour and then saturated again with hydrogen chloride. The resulting liquid was allowed to stand overnight and then was shaken vigorously with excess 40 per cent sodium hydroxide solution for approximately one-half hour. The two layers were separated and the upper layer was washed with water. The product was dried over anhydrous magnesium sulfate and distilled under reduced pressure, b.p. 140-145°C. at 12-15 mm. pressure. The yield was 10 g. (40 per cent).

Treatment with 2,4-dinitrophenylhydrazine according to the procedure of Johnson (12) yielded two products. Separation of these two products by fractional crystallization yielded an orange derivative, m.p. 145.5-147°C. as the major product, and a yellow derivative, m.p. 108-113°C. (impure). Analysis. Calculated for $C_{18}H_{22}O_4N_4$: C, 60.3; H, 6.2; N, 15.6. Found: C, ; H .

Preparation of 2-Cyclohexylcyclohexanone

Redistilled 2-cyclohexenylcyclohexanone (II) (0.1 mole) was immediately dissolved in absolute ethanol, 5-6 g. of 10 per cent palladium-charcoal were added, and the mixture was placed under forty pounds per square inch of hydrogen at 80-100°C. with shaking. The theoretical amount of hydrogen (10 p.s.i.) was absorbed over a period of approximately three hours. The material was removed from the hydrogenation apparatus, filtered, and the ethanol removed by distillation. The resulting liquid gave negative results with potassium

permanganate and bromine in carbon tetrachloride and a positive reaction with 2,4-dinitrophenylhydrazine.

Preparation of Methyl 2-Cyclohexyl-1-hydroxycyclohexyl-
acetate (III)

Approximately 50 ml. of anhydrous, thiophene-free benzene and 9 g. (.05 moles) of crude 2-cyclohexylcyclohexinone were placed in a dry, three-neck flask fitted with a stirrer, condenser, and separatory funnel and protected from moisture with calcium chloride tubes. The solution was then refluxed with stirring and 11.5 g. (.075 moles) of methyl bromoacetate were added dropwise over a period of 45 minutes, while small portions of dry, clean, 20 mesh zinc metal were added every 5-10 minutes. This mixture was then refluxed for an additional two hours with stirring and then cooled in an ice water bath. The complex was decomposed by addition of a mixture of 50 ml. of glacial acetic acid and 50 ml. of water, followed by addition of 120 ml. of ice water. The product was extracted three times with ether and the combined ether layers washed four times with approximately 2.5 per cent ammonium hydroxide. The combined washings were extracted once with ether and the combined ether layers were dried over anhydrous magnesium sulfate. The ether was removed by distillation under reduced pressure and 6.6 g. (51.6 per cent based on 2-cyclohexenylcyclohexanone) of crude product was obtained, m.p. 55-59°C. Recrystallization from

methanol-water yielded colorless needles, m.p. 59-60°C. The compound gave negative results with potassium permanganate and bromine in carbon tetrachloride. Analysis. Calculated for $C_{15}H_{26}O_3$: C, 70.8; H, 10.3. Found: C, ; H, .

Preparation of 2-Cyclohexyl-1-hydroxy-
cyclohexylacetic Acid (IV)

Two grams of methyl 2-cyclohexyl-1-hydroxycyclohexylacetate were placed in a flask containing 90 ml. of methanol and 50 ml. of 5 per cent sodium hydroxide. The resulting solution was refluxed for 30 minutes. The liquid was evaporated to a volume of about 50 ml., extracted with ether and acidified to litmus with 10 per cent hydrochloric acid. The precipitate was filtered and recrystallized from benzene. The yield was 1.81 g. (95 per cent). This acid is a colorless solid, m.p. 137.5-139°C.

A neutralization equivalent indicated a molecular weight of 241 \pm 1 (calculated molecular weight 240). The compound gave negative results with potassium permanganate and with bromine in carbon tetrachloride. Analysis. Calculated for $C_{14}H_{24}O_3$: C, 70.0; H, 10.1. Found: C, ; H, .

Preparation of Methyl 2-Cyclohexylcyclo-
hexenylacetate (V)

In a dry three-neck flask fitted with a stirrer and a condenser and protected by a calcium chloride tube, were placed 50 ml. of anhydrous, thiophene-free benzene and 3 g.

of methyl 2-cyclohexyl-1-hydroxycyclohexylacetate (III). The solution was heated to boiling with stirring and 5 g. of phosphorous pentoxide was added in small portions over a period of one hour. The mixture was refluxed for an additional hour and was then treated with 150 ml. of ice water. This mixture was extracted three times with ether and the ether layers washed with water. The combined ether layers were dried over anhydrous magnesium sulfate, filtered, and the ether removed by distillation. Vacuum distillation of the resulting liquid yielded 2.3 g. (82 per cent) of colorless liquid, boiling at 146-152°C./4-6 mm. This liquid turned pale yellow on standing. The compound gave a slow reaction with potassium permanganate and a rapid reaction with bromine in carbon tetrachloride with the evolution of hydrogen bromide.

Into a solution of one ml. of pyridine in 10 ml. of ether was placed .472 g. of methyl 2-cyclohexyl-1-hydroxycyclohexylacetate (III). The solution was cooled in an ice bath and one ml. of thionyl chloride was added dropwise with stirring. The mixture was allowed to stand overnight and then mixed with 30 ml. of water to which 5 drops of hydrochloric acid had been added. To the resulting mixture 25 ml. of ether were added and the layers separated. The ether layer was washed with water and then dried over anhydrous magnesium sulfate. The ether extract was filtered

and the ether was removed by distillation under reduced pressure yielding a quantitative amount of starting material.

Preparation of 2-Cyclohexylcyclohexenylacetic Acid (VI)

The procedure used for the preparation of methyl 2-cyclohexylcyclohexenylacetate (V) was followed with 2 g. of 2-cyclohexyl-1-hydroxycyclohexylacetic acid (IV) and 3.5 g. of phosphorous pentoxide. Vacuum distillation yielded 1.3 g. (71 per cent) of colorless liquid, boiling point 175-180°C./4-6 mm.

A solution of 25 ml. of methanol, 1 g. of methyl 2-cyclohexylcyclohexenylacetate (V), and .256 g. of sodium hydroxide was refluxed for 30 minutes after which most of the methanol was removed by distillation. Acidification with 10 per cent hydrochloric acid followed by extraction with ether, drying of the ether, and distillation yielded .86 g. (91 per cent) of colorless liquid, boiling point 174-180°C./4-6 mm.

This acid turned pale yellow upon standing. It gave a slow reaction with potassium permanganate and a rapid reaction with bromine in carbon tetrachloride with the evolution of hydrogen bromide. It formed a solid p-bromophenacylester, m.p. 81-82°C. from ethanol. Analysis. Calculated for $C_{22}H_{27}O_3Br$: C, 63.0; H, 6.5. Found: C, ; H, .

Dehydrogenation Attempts with Methyl 2-Cyclohexylcyclohexenylacetate (V) and Methyl 2-cyclohexyl-1-hydroxycyclohexylacetate (VI)

All attempts to dehydrogenate these compounds in the usual manner were unsuccessful. Heating with palladium-charcoal from 200-350°C. for 1-8 hours yielded no isolable product.

A small amount of methyl 2-cyclohexylcyclohexenylacetate (V) was placed in a length of 8 mm. pyrex glass tubing on a column of 10 per cent palladium-charcoal about 3 cm. high. The tube was placed in a Wood's metal bath at 300-350°C. for 8 hrs., extracted with ether, filtered, and distilled. An oil was obtained which yielded a picrate which was quite impure. Repeated fractional crystallization yielded a small amount of picrate, m.p. 138-141°C. from ethanol.

Dehydrogenation of 2-Cyclohexylcyclohexenylacetic Acid (VI)

Into a test tube containing 1-2 g. of 10 per cent palladium-charcoal was placed 0.700 g. of 2-cyclohexylcyclohexenylacetic acid. This mixture was heated in a Wood's metal bath at 250-300°C. for two hours and at 300-350°C. for six hours. The reaction product was taken up in ether, filtered, and the ether extracted three times with 10 per cent sodium bicarbonate solution. The ether was then removed by distillation and a crude oil was obtained.

Acidification of the sodium bicarbonate extract with 10 per cent hydrochloric acid yielded about 40 mg. of a colorless acid, probably biphenyl-2-acetic acid, m.p. 111-113°C. after recrystallization from ethanol. The reported melting point is 115°C. (Schonberg and Warren, 20).

Vacuum distillation of the non-acidic oil yielded 280 mg. of 2-methylbiphenyl, boiling point 95-100°C./0.5-0.7 mm.

The distilled 2-methylbiphenyl was placed in a flask containing 30 ml. of water and 0.8 g. of potassium permanganate. This mixture was refluxed for one and one-half hours and the excess potassium permanganate destroyed by addition of sodium bisulfite. The solution was then filtered, extracted with ether, and acidified with 10 per cent hydrochloric acid. About 20 mg. of o-phenylbenzoic acid was isolated, m.p. 106-108°C. after recrystallization from an alcohol-water mixture. The reported melting point is 110°C. (Jacobsen, 11).

Further distillation of the crude dehydrogenation oil yielded about 100 mg. of phenanthrene, boiling point 125-140°C./0.3-0.5 mm. Recrystallization from ethanol yielded colorless crystals, m.p. 96-97°C., reported 100°C. (Shriner and Fuson, 21). Treatment with picric acid yielded a crystalline picrate, m.p. 143-143.5°C., reported 144°C. (Shriner and Fuson, 21).

Preparation of $\Delta^{10,11}$ -Perhydro-9-phenanthrone (IX)

A mixture of 10 ml. of polyphosphoric acid and 2 g. of methyl 2-cyclohexyl-1-hydroxycyclohexylacetate (III) was heated on a steam bath with swirling until all of the solid had dissolved and then for an additional 2-3 minutes. The solution was then placed in an oil bath at 115-120°C. for 3-4 minutes, cooled, and about 100 ml. of water added. The resulting mixture was extracted twice with ether, the ether layers washed with water, and dried over anhydrous magnesium sulfate. The ether solution was filtered and the ether was removed by distillation. Vacuum distillation of the resulting oil yielded 0.8 g. of oil boiling at 120-140°C./4-6 mm. and 0.8 g. (49.3 per cent) of a substance, probably $\Delta^{10,11}$ -perhydro-9-phenanthrone (IX), boiling at 170-190°C./4-6 mm., 2,4-dinitrophenylhydrazone (Johnson, 12) m.p. 225-226.5°C., reported 226-227°C. (Pinkney, et al, 16).

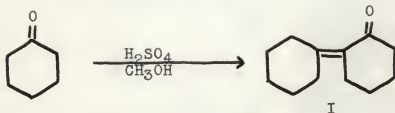
To obtain seed crystals a chromatogram was made of the material dissolved in hexane on an activated silica column. The column was developed with Skelly B and eluted with benzene after which the solvent was removed by evaporation. The first fractions contained little material, but this was followed by a band which yielded the major portion of the desired ketone (IX), which spontaneously crystallized upon standing for two days, m.p. 78-81°C. Crystallization from _____ yielded colorless crystals, m.p. _____ C., reported 89°C. (Pinkney, et al, 16).

Spectra

The ultra-violet absorption spectra of 2-cyclohexenylcyclohexanone-2,4-dinitrophenylhydrazone and Δ^{10} -perhydro-9-phenanthrone-2,4-dinitrophenylhydrazone were obtained in chloroform solution with a Beckmann Model DU spectrophotometer with a one cm. cell and using maximum sensitivity.

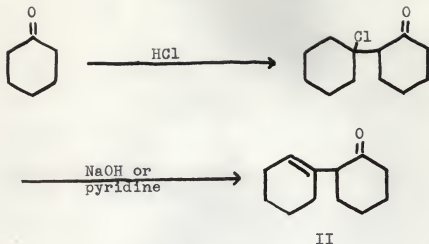
DISCUSSION

In 1907 Mannich (14) reported the preparation of 2-cyclohexylidenecyclohexanone (I) by the condensation of two moles of cyclohexanone in methanolic sulfuric acid.



Gault, et al, (9) reported the same compound using 60 per cent aqueous sulfuric acid. Both of these procedures were reported to give good yields, generally being 80 per cent or better.

However, Rapson (18) reported that saturation of cyclohexanone with anhydrous hydrogen chloride, followed by treatment with sodium hydroxide or pyridine yielded the theoretical amount of 2-cyclohexenylcyclohexanone (II).



These three procedures were followed and it was found that Rapson's method was not only the easiest, but afforded the best yield, although a quantitative yield of product was never approached.

Treatment of the product obtained by the procedure of Rapson with 2,4-dinitrophenylhydrazine reagent yielded two products, an orange derivative and a yellow derivative. These products were separated difficultly by fractional crystallization, but the yellow derivative (the more insoluble of the two) could not be isolated in pure form as it was transformed to the orange derivative upon warming in ethanol, the crystallization solvent.

The ultra-violet spectra of these two derivatives were then taken (Plate I). The two compounds gave identical spectra with absorption maxima at 370 $m\mu$ indicating unconjugation (4), (6), (19).

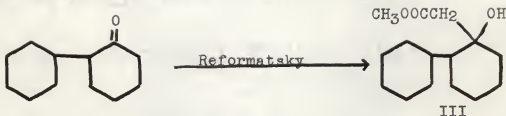
Since these two derivatives are not isomers with respect to the position of the carbon-carbon double bond and yet have rather widely differing melting points, it seems likely that they are isomers involving the carbon-nitrogen double bond. It also seems likely that the yellow compound is the *cis*- compound, since it is converted to the orange compound by warming in ethanol and it is well-known that *trans*- compounds are generally more stable than their *cis*- isomers. The fact that the *cis*- compound has a good deal lighter color than the *trans*- in the solid state is then reasonable from probable steric factors. Apparently the cyclohexyl ring interferes with the aromatic ring in such a way as to force it somewhat out of the plane of the double bond and thus decrease the resonance of the system. This may be correlated with the fact that the yellow derivative can only be isolated, and then in impure form, from a solution containing a large excess of the orange, or *trans*-, derivative. Apparently the equilibrium set up between the two forms in ethanol or in chloroform (spectral solvent) is so far in favor of the *trans*- form that at the dilution used for the spectra (about 1 mg./100 ml.), the *cis*- form is not present in high enough concentration to significantly affect the observed spectrum.

Rapson (18) reported that 2-cyclohexenylcyclohexanone (II) could be reduced rapidly by hydrogen using palladium on strontium carbonate to yield 2-cyclohexylcyclohexanone.

It was found, however, that 2-cyclohexenylcyclohexanone decomposed slightly on standing and attempts to hydrogenate this slightly impure compound with palladium-charcoal, platinum, or Raney nickel were all unsuccessful. During the course of these experiments solvents used were 95 per cent ethanol, absolute ethanol, and absolute ethanol containing a few drops of hydrochloric acid.

The hydrogenation was accomplished finally by redistilling the 2-cyclohexenylcyclohexanone, immediately adding five to six grams of ten per cent palladium-charcoal, and hydrogenating this mixture at forty pounds per square inch pressure and heating to 80-100°C. This material slowly absorbed hydrogen (approximately three pounds pressure drop per hour).

2-Cyclohexylcyclohexanone reacts smoothly with methyl bromoacetate in the presence of zinc metal in a typical Reformatsky reaction to yield methyl 2-cyclohexyl-1-hydroxy-cyclohexylacetate (III).

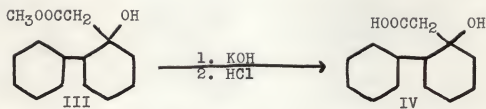


The procedure used was essentially that of Bachmann and Dreiding (1). A small amount of iodine was added as an initiator and the zinc and methyl bromoacetate were added in small portions as the reaction progressed. The reaction

exhibited an induction period of approximately 15-30 minutes, after which it proceeded vigorously with the production of the grayish-green color typical of the Reformatsky reaction. Continued refluxing was necessary to obtain good yields, however, and at the end of the reflux period the solution was a dark gray color. The 2-cyclohexylcyclohexanone was not purified after hydrogenation except to remove the hydrogenation solvent by distillation. The crude material was then subjected to the Reformatsky reaction and the overall yield from 2-cyclohexenylcyclohexanone was slightly over 50 per cent.

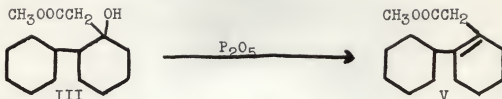
The initial reaction after the induction period is often quite vigorous and care must be taken to control it. As this first reaction subsides the remaining portion reacts smoothly.

Treatment of methyl 2-cyclohexyl-1-hydroxycyclohexylacetate (III) with methanolic sodium hydroxide followed by acidification with dilute hydrochloric acid gave a nearly quantitative yield of 2-cyclohexyl-1-hydroxycyclohexylacetic acid (IV).



Treatment of methyl 2-cyclohexyl-1-hydroxycyclohexylacetate (III) with phosphorous pentoxide in refluxing benzene

was found to give a good yield (65-85 per cent) of methyl 2-cyclohexylcyclohexenylacetate (V).



This unsaturated ester is a high boiling, colorless liquid which gives a slow reaction with potassium permanganate and a rapid reaction with bromine in carbon tetrachloride with the evolution of hydrogen bromide. On standing it decomposes slightly with the appearance of a pale yellow color. The infra-red spectrum of this compound showed a carbon-carbon double bond absorption at 6.01μ , which indicates lack of conjugation with the ester carbonyl. The carbonyl absorption band was present at 5.74μ .

The structure V would be expected to be correct rather than Va or Vb from these results. The fact that bromine substituted rather than following the usual course of addition may then be explained. The structure Va would be expected

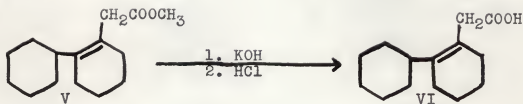


to add bromine in the usual manner and furthermore, does not fit the spectral data. Structure Vb would be expected to fit the experimental facts, and may be correct. However,

the double bond is usually formed in such a manner that it becomes as substituted as possible, thus making structure V the most likely. The carbon alpha to the carbonyl group is double activated to substitution, both by the carbonyl and the double bond, thus making it reasonable that substitution should occur. The addition, as is shown by the slow reaction with potassium permanganate, is apparently hindered by the bulk of the attached groups, thus slowing it a good deal and allowing substitution to predominate.

During the course of these experiments it was found that the hydroxyl group was unexpectedly resistant to dehydration. The material can be distilled unchanged and treatment with thionyl chloride and pyridine following the method of Bachmann and Dreiding (1) failed to accomplish the dehydration.

The preparation of 2-cyclohexylcyclohexenylacetic acid (VI) was accomplished by two methods. Treatment of methyl 2-cyclohexylcyclohexenylacetate (V) with methanolic potassium hydroxide resulted in a nearly quantitative yield of the acid.



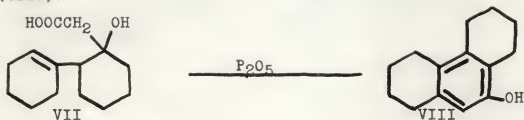
Dehydration of 2-cyclohexyl-1-hydroxycyclohexylacetic acid (IV) with phosphorous pentoxide in the same manner as

with the corresponding ester yielded 70-75 per cent of the theoretical amount of the unsaturated acid.

This compound is a viscous oil which could not be crystallized. It reacts slowly with potassium permanganate and rapidly with bromine in carbon tetrachloride with the evolution of hydrogen bromide. On standing it decomposes slightly with the formation of a pale yellow color.

The infra-red spectrum of the compound showed an associated acid oxygen-hydrogen stretching band at 3.71μ , a broad unassociated acid oxygen-hydrogen stretching band at 2.97μ to 3.16μ , a carbonyl absorption at 5.87μ , and a carbon-carbon double bond absorption at 6.04μ (unconjugated).

Bagchi et al, (2) reported that treatment of 2-cyclohexenyl-1-hydroxycyclohexylacetic acid (VII) with phosphorous pentoxide yields 1,2,3,4,5,6,7,8-octahydro-9-phenanthrol (VIII).



From the results obtained in this work it appears that the presence of the double bond in the 2-cyclohexyl group is a necessary requirement for this ring closure to be accomplished.

All attempts to dehydrogenate either methyl 2-cyclohexyl-1-hydroxycyclohexylacetate (III) or methyl 2-cyclohexyl-

cyclohexenylacetate (V) were unsuccessful with respect to isolating any practical amount of identifiable material. The methyl 2-cyclohexyl-1-hydroxycyclohexylacetate (III) dehydrated at high temperatures in the presence of 10 per cent palladium-charcoal but the products obtained were intractable oils which could not be identified. Methyl 2-cyclohexylcyclohexenylacetate (V) boils at a temperature considerably below efficient dehydrogenation temperatures. This results in violent spattering and bumping when the condensed liquid comes in contact with the heated catalyst, and immediate volatilization of the liquid. Oils were the only isolable products obtained. Various temperature ranges and periods of contact were attempted during these experiments, but no results could be obtained with any of the conditions tried. Dehydrogenation was attempted with sulfur, also, but again no identifiable product was obtained.

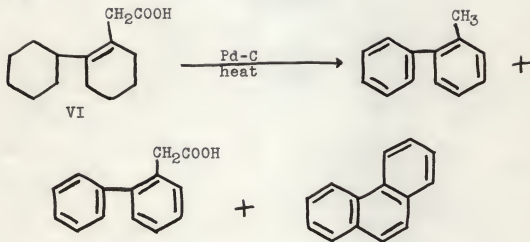
However, an attempt to dehydrogenate a small amount of methyl 2-cyclohexylcyclohexenylacetate (V) was made in a length of 8 mm. pyrex glass tubing and an oil was obtained which formed a picrate. Apparently there were several products present because the picrate was quite impure. Repeated fractional crystallization yielded a substance, m.p. 138-141°C., which is probably phenanthrene picrate (reported m.p. 144°C. (Shriner and Fuson 21)).

The failure of this reaction to yield the expected product is probably due to the low boiling character of the

unsaturated ester. It is likely that vapor phase dehydrogenation would succeed.

Attempts to hydrogenate methyl 2-cyclohexylcyclohexenylacetate (V) at low pressures using palladium-charcoal, platinum, or Raney nickel and heating were all unsuccessful. These results may be due to steric hindrance present in the compound or to the presence of impurities.

The dehydrogenation of 2-cyclohexylcyclohexenylacetic acid (VI) proceeded quite well, forming three different products. Besides the expected 2-methylbiphenyl, a small amount of acid was isolated, which was probably biphenyl-2-acetic acid, although too small an amount was obtained for efficient purification. Phenanthrene was also obtained in low yield.



From the non-acidic material 2-methylbiphenyl was isolated in much the largest amount of the three products. This product was identified by treatment with potassium

(Plate I) showed a maximum at 395 $m\mu$, indicating conjugation of the double bond (6), (13), (15).

The ketone was reported as a solid (Pinkney, et al 16), but the crude oil obtained resisted ordinary attempts to crystallize it. The substance obtained was a rather complex mixture as was shown by a chromatogram of the material. Three fluorescent bands were observed and at least one non-fluorescent band was obtained. The first fraction obtained upon elution of the column was a colorless oil which crystallized upon standing. This material proved to be $\Delta^{9,10}$ -perhydro-9-phenanthrone (IX).

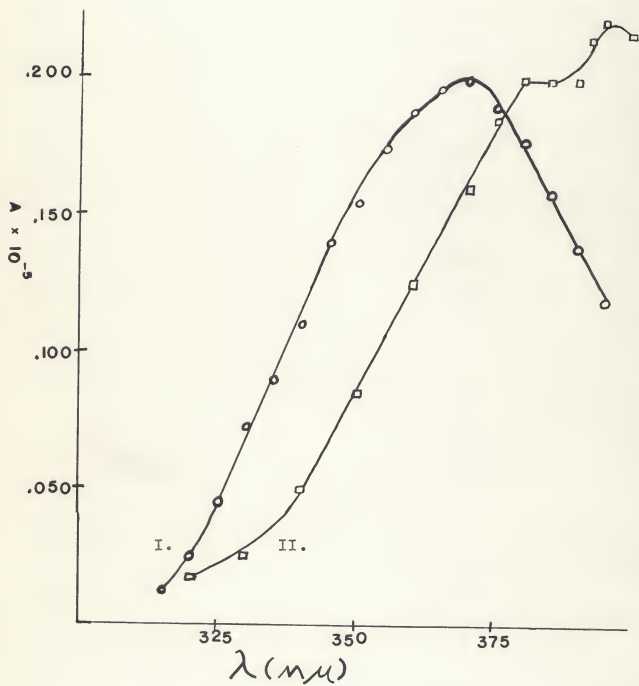
This compound might prove to be an intermediate in the preparation of 9-substituted phenanthrenes through hydrogenation of the double bond followed by Grignard reaction of the keto group, dehydration, and dehydrogenation. This leads to the 2,6,10- and 1,5,9- trisubstituted phenanthrenes if substituted cyclohexanones are used in the first step of the synthesis.

EXPLANATION OF PLATE I

Ultra-violet absorption spectra

- I. 2-Cyclohexenylcyclohexanone-2,4-dinitrophenylhydrazone.
- II. $\Delta^{10,11}$ -perhydro-9-phenanthrone-2,4-dinitrophenylhydrazone.

PLATE I



SUMMARY

Methyl 2-cyclohexyl-1-hydroxycyclohexylacetate and 2-cyclohexyl-1-hydroxycyclohexylacetic acid have been synthesized by means of a Reformatsky reaction starting with 2-cyclohexylcyclohexanone. These hydroxy compounds have been found to be exceptionally resistant to the usual dehydration reactions.

Methyl 2-cyclohexylcyclohexenylacetate and 2-cyclohexylcyclohexenylacetic acid have been prepared by treatment of the corresponding hydroxy compounds with phosphorous pentoxide. It was found that methyl 2-cyclohexylcyclohexenylacetate could not be dehydrogenated by the usual methods, although the corresponding acid underwent dehydrogenation in the expected manner.

It has been found that treatment of 2-cyclohexyl-1-hydroxycyclohexylacetic acid with phosphorous pentoxide does not yield a tricyclic compound such as Bagchi (2) obtained using 2-cyclohexenyl-1-hydroxycyclohexylacetic acid. This indicates that the double bond is a necessary requirement for this ring closure.

$\Delta^{10,H}$ -perhydro-9-phenanthrone has been prepared by treatment of methyl 2-cyclohexyl-1-hydroxycyclohexylacetate with polyphosphoric acid, thus leading to the possible synthesis of 1,5,9- and 2,6,10- trisubstituted phenanthrenes.

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ACID CATALYZED CONDENSATIONS OF CYCLIC
KETONES: I. ATTEMPTED SYNTHESIS OF
PHENANTHRENE

by

JOHN EDWARD KATON

B. S., Bowling Green State
University, 1951

AN ABSTRACT OF A THESIS

submitted in partial fulfillment of

requirements for the degree

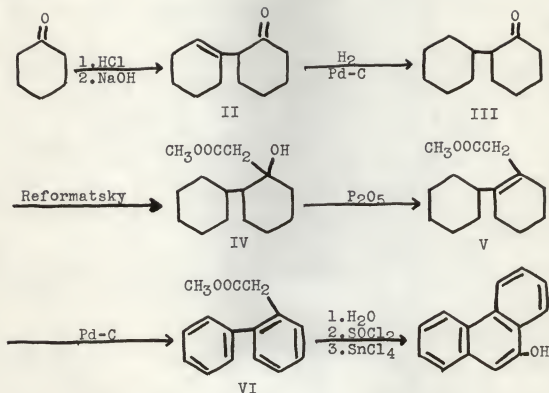
MASTER OF SCIENCE

Department of Chemistry

KANSAS STATE COLLEGE
OF AGRICULTURE AND APPLIED SCIENCE

1955

An attempt to synthesize 9-phenanthrol was made following the route:



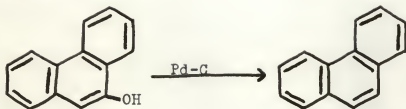
However, it was found that the dehydrogenation step presented difficulties which would require extended work to overcome.

2-Cyclohexenylcyclohexanone (II) was prepared by the hydrogen chloride catalyzed condensation of cyclohexanone, followed by dehydrohalogenation. This compound was difficultly reduced to 2-cyclohexylcyclohexanone (III) and this material was subjected to the Reformatsky reaction to produce methyl 2-cyclohexyl-1-hydroxycyclohexylacetate (IV) in 52 per cent yield based on 2-cyclohexenylcyclohexanone (II).

It was found that IV was surprisingly difficult to dehydrate by the usual methods, but treatment with phosphorous pentoxide yielded 82 per cent of methyl 2-cyclohexylcyclohexenylacetate (V).

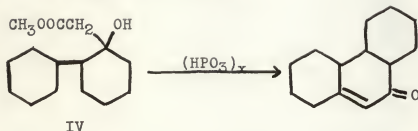
The ester V was found to boil at a temperature too low for efficient dehydrogenation and thus could not be converted to methyl biphenyl-2-acetate.

However, the corresponding acid could be dehydrogenated smoothly to yield a mixture of products. The main product of this reaction was the expected 2-methylbiphenyl. There was also obtained some phenanthrene, which indicates that the reaction



will occur.

It was found that ring closure of methyl 2-cyclohexyl-1-hydroxycyclohexylacetate (IV) could be effected by treatment with polyphosphoric acid.



This compound might lead to 9-substituted phenanthrenes by further typical synthetic procedures. Since 2- and 4-substituted cyclohexanones should undergo the primary condensation, this procedure leads to a possible new route to 2,6,10- and 1,5,9- trisubstituted phenanthrenes, as well as 2,6- and 1,5- disubstituted and 9- monosubstituted phenanthrenes.

